

REMARKS

Priority Claim:

The specification has been amended to include the priority claim.

Claim Amendments:

Claim 1 has been narrowed by amendment to cover the use of *ortho*-halo-2-aminonaphthalines as starting substrates. More particularly, Claim 1, as amended, now covers the processes of Groups I and II only, viz, the allylation of *ortho*-halo-2-aminonaphthalines and the cyclization of a vinyl chloride product for producing the dihydroindole C-ring of CC-1065/duocarmycin analogs.

Election/Restriction:

Applicant continues to traverse a portion of the Examiner's Election/Restriction Requirement. Claim 1 has been amended so as to include support for the synthesis of both compounds 12 (a) and 12 (b). More generally, Claim 1 is directed to a genus process that employs *ortho*-halo-2-aminonaphthalines as a starting substrate for synthesizing the dihydroindole C-ring of CC-1065/duocarmycin analogs. The chemistry of the allylation process for *ortho*-halo-2-aminonaphthalines are similar and form one class. Furthermore, the cyclization properties of the resultant vinyl chloride are also similar and forms one class. Application requests that the Examiner reconsider the Election/Restriction requirement in view of this amendment. More particularly, it is requested that Groups I and II be merged in view of Applicant's amendment to Claim 1.

Rejection under 35 USC 112, first paragraph:

Claim 1 is rejected under 35 USC 112, first paragraph, for lack of enabling support. The Examiner suggests that the specific reaction conditions at the bottom of page 4 of the specification be included in Claim 1. Applicant traverses this basis for rejection. Claim 1 is to be read in light of the specification, including the reaction conditions at the bottom of page 4 of the specification. Claim is fully enabled by the specification. Withdrawal of this basis for rejection is requested.

Claim 32:

Claim 32 is an independent species claim, previously presented, covering a process for synthesizing compound 12a. Claim 32 represents a merger of claims 1 and 26. The Office Action, dated 03/25/2003, does not appear to have included an examination of Claim 32. Examination of Claim 32 is requested.

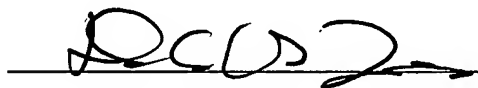
Summary:

Claims 1 and 19-20 have been amended. Applicant requests that the Examiner reconsider the election/restriction requirement in view of the amendments to Claim 1. More particularly, Applicant requests that Groups I and II be merged. Withdrawal of the enablement rejection with respect to Claim 1 is requested. Examination of claims 1, 19-20, 22-27, and 32 is requested.

Respectfully submitted,

Sept 25, 2003

Date



Donald G. Lewis, Reg. No. 28,636

THE SCRIPPS RESEARCH INSTITUTE

Office of Patent Counsel

10550 North Torrey Pines Road

Mail Drop: TPC-8

La Jolla, California 92037

September 25, 2003

(858) 784-2937

APPENDIX I

VERSION OF SPECIFICATION WITH MARKINGS TO SHOW CHANGES MADE

A marked-up version of amendments to the specification is provided:

In the Specification:

Page 1, after the Title and prior to the Technical Field, please insert the following new paragraph:

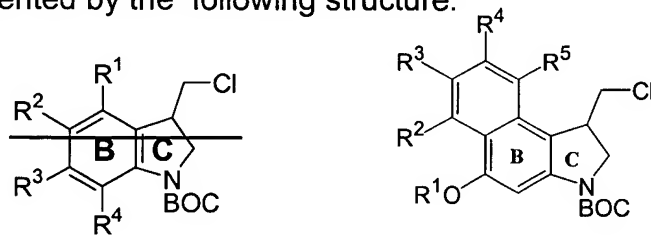
Cross-Reference to Related Applications:

This is a divisional application of copending U.S. patent application Serial No. 09/581,049, filed July 10, 2000, which issued on October 30, 2001 as U.S Patent No. 6,310,209 B1, which is a US national phase application of international application Serial No. PCT/US98/25992, filed December 8, 1998 and published in English, which claims priority from and is a continuation-in-part of US provisional application application Serial No. 60/067,960, filed December 8, 1997.

APPENDIX II

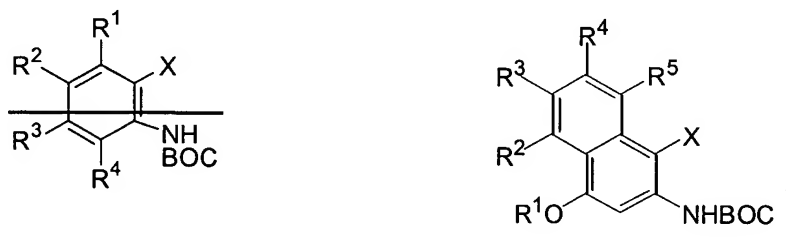
RESTATEMENT OF ALL CLAIMS WITH MARKINGS TO SHOW CHANGES MADE TO PRESENTLY AMENDED CLAIMS

1. (presently amended) A process for synthesizing a dihydroindole C-ring of a CC-1065/duocarmycin analog, the dihydroindole C-ring of a CC-1065/duocarmycin analog being represented by the following structure:



the process comprising the following steps:

Step A: allylating an ~~ortho-haloaniline~~ ortho-halo-2-aminonaphthalene with 1,3-dichloropropene for forming a vinyl chloride, the ~~ortho-haloaniline~~ ortho-halo-2-aminonaphthalene being represented by the following structure:



wherein:

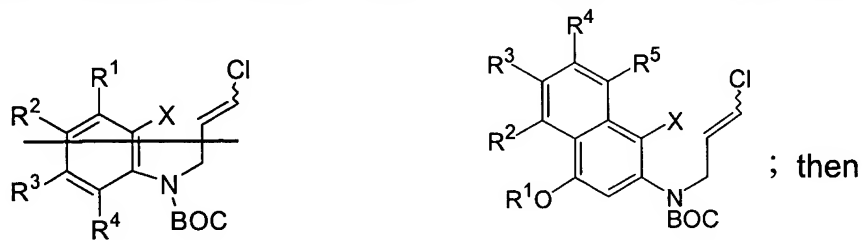
R¹ is a hydroxyl protecting group; and

R², R³, and R⁴, and R⁵ are radicals independently selected from the group consisting of hydrogen, alkyl(C1-C6), alkoxy, cyano, and arylalkoxy, ~~with a proviso that R¹ and R², or R² and R³ may form a fused 5- or 6-membered ring with or without a heteroatom; and~~

X is a halide selected from the group consisting of bromine and iodine; and the vinyl chloride is represented by the following structure:

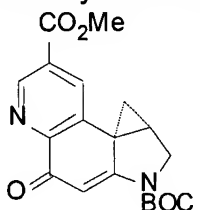
APPENDIX II

RESTATEMENT OF ALL CLAIMS WITH MARKINGS TO SHOW CHANGES MADE TO PRESENTLY AMENDED CLAIMS

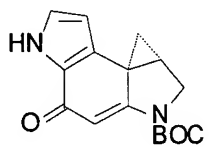


Step B: cyclizing the vinyl chloride of said step A for forming the dihydroindole C-ring of the CC-1065 /duocarmycin analog.

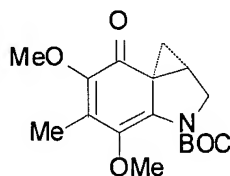
2. (withdrawn) A compound represented by the following structure:



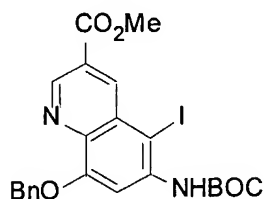
3. (withdrawn) A compound represented by the following structure:



4. (withdrawn) A compound represented by the following structure:



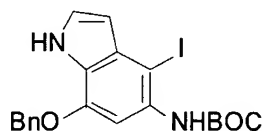
5. (withdrawn) A compound represented by the following structure:



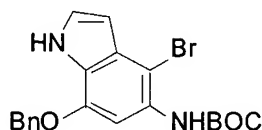
APPENDIX II

RESTATEMENT OF ALL CLAIMS WITH MARKINGS TO SHOW CHANGES MADE TO PRESENTLY AMENDED CLAIMS

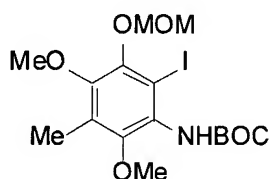
6. (withdrawn) A compound represented by the following structure:



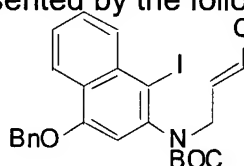
7. (withdrawn) A compound represented by the following structure:



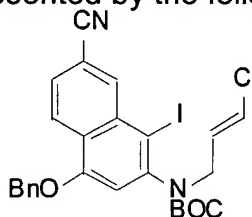
8. (withdrawn) A compound represented by the following structure:



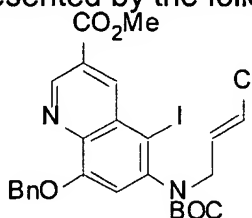
9. (withdrawn) A compound represented by the following structure:



10. (withdrawn) A compound represented by the following structure:



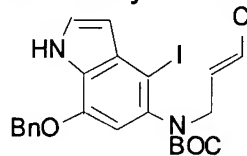
11. (withdrawn) A compound represented by the following structure:



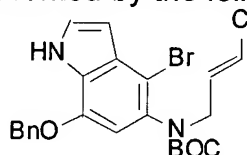
APPENDIX II

RESTATEMENT OF ALL CLAIMS WITH MARKINGS TO SHOW CHANGES MADE TO PRESENTLY AMENDED CLAIMS

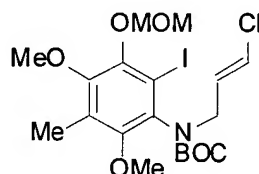
12. (withdrawn) A compound represented by the following structure:



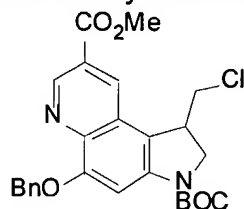
13. (withdrawn) A compound represented by the following structure:



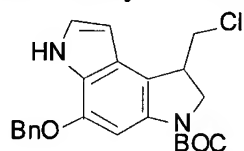
14. (withdrawn) A compound represented by the following structure:



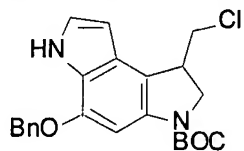
15. (withdrawn) A compound represented by the following structure:



16. (withdrawn) A compound represented by the following structure:



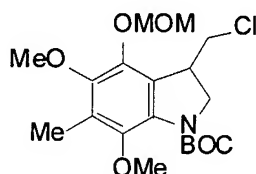
17. (withdrawn) A compound represented by the following structure:



18. (withdrawn) A compound represented by the following structure:

APPENDIX II

RESTATEMENT OF ALL CLAIMS WITH MARKINGS TO SHOW CHANGES MADE TO PRESENTLY AMENDED CLAIMS



5 19. (presently amended) A process according to claim 1 wherein, in said Step A, the ~~ortho-haloaniline~~ ortho-halo-2-aminonaphthalene is an ~~ortho-bromoaniline~~ ortho-bromo-2-aminonaphthalene.

10 20. (presently amended) A process according to claim 1 wherein, in said Step A, the ~~ortho-haloaniline~~ ortho-halo-2-aminonaphthalene is an ~~ortho-iodoaniline~~ ortho-iodo-2-aminonaphthalene.

15 21. (cancelled) A process according to claim 1 wherein, in said Step A, the *ortho*-haloaniline is protected with a BOC group.

22. (previously added) A process according to claim 1 wherein, in said Step A, said allylation is catalyzed by the addition of a catalytic amount of tetra-*n*-butylammonium iodide.

20 23. (previously added) A process according to claim 1 wherein, in said Step B, said cyclization is performed with an addition of tri-*n*-butyltin hydride.

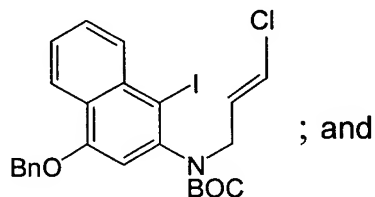
24. (previously added) A process according to claim 23 wherein, in said Step B, said cyclization is catalyzed by the addition of a catalytic amount of AIBN.

25 25. (previously added) A process according to claim 24 wherein, in said Step B, said cyclization is performed using toluene as the solvent.

APPENDIX II

RESTATEMENT OF ALL CLAIMS WITH MARKINGS TO SHOW CHANGES MADE TO PRESENTLY AMENDED CLAIMS

26. (previously added) A process according to claim 1 wherein, in said Step A, the vinyl chloride is represented by the following structure:



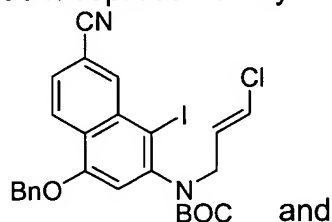
in said Step B, the dihydroindole C-ring of the CC-1065/duocarmycin analog is represented by the following structure:



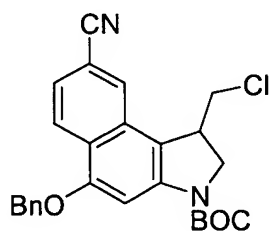
15

27. (previously added) A process according to claim 1 wherein:

in said Step A, the vinyl chloride is represented by the following structure:



in said Step B, the dihydroindole C-ring of the CC-1065 / duocarmycin analog is represented by the following structure:

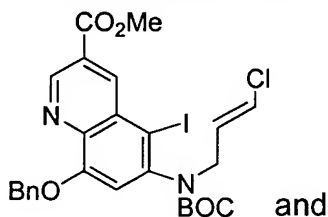


APPENDIX II

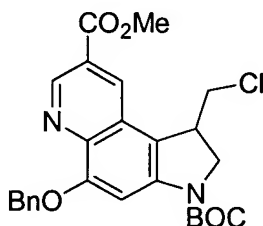
RESTATEMENT OF ALL CLAIMS WITH MARKINGS TO SHOW CHANGES MADE TO PRESENTLY AMENDED CLAIMS

28. (cancelled) A process according to claim 1 wherein:

in said Step A, the vinyl chloride is represented by the following structure:

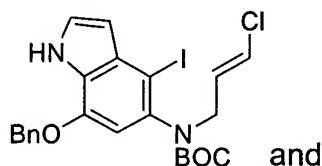


in said Step B, the dihydroindole C-ring of the CC-1065 / duocarmycin analog is represented by the following structure:

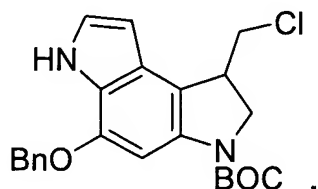


29. (cancelled) A process according to claim 1 wherein:

in said Step A, the vinyl chloride is represented by the following structure:



in said Step B, the dihydroindole C-ring of the CC-1065 / duocarmycin analog is represented by the following structure:

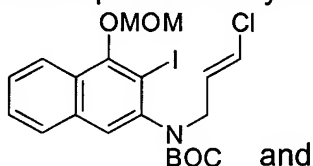


APPENDIX II

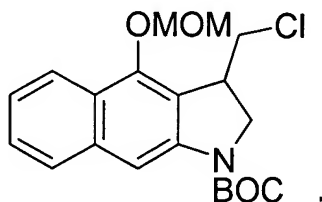
RESTATEMENT OF ALL CLAIMS WITH MARKINGS TO SHOW CHANGES MADE TO PRESENTLY AMENDED CLAIMS

30. (cancelled) A process according to claim 1 wherein:

in said Step A, the vinyl chloride is represented by the following structure:

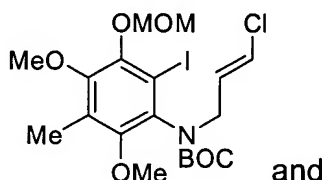


in said Step B, the dihydroindole C-ring of the CC-1065 / duocarmycin analog is represented by the following structure:

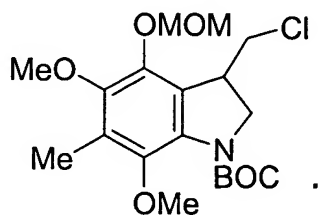


31. (cancelled) A process according to claim 1 wherein:

in said Step A, the vinyl chloride is represented by the following structure:



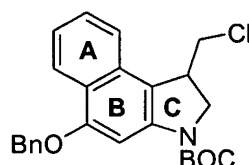
in said Step B, the dihydroindole C-ring of the CC-1065 / duocarmycin analog is represented by the following structure:



APPENDIX II

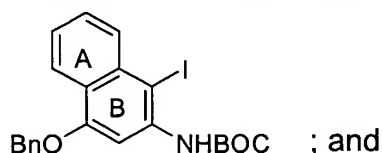
RESTATEMENT OF ALL CLAIMS WITH MARKINGS TO SHOW CHANGES MADE TO PRESENTLY AMENDED CLAIMS

32. (previously added) A process for synthesizing a dihydroindole C-ring of a CC-1065/duocarmycin analog, the dihydroindole C-ring of a CC-1065/duocarmycin analog being represented by the following structure:

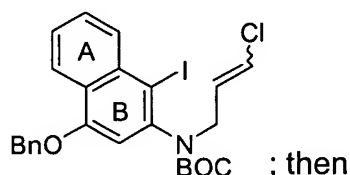


the process comprising the following steps:

Step A: allylating an *ortho*-haloaniline with 1,3-dichloropropene for forming a vinyl chloride, the *ortho*-haloaniline being represented by the following structure:



the vinyl chloride being represented by the following structure:



Step B: cyclizing the vinyl chloride of said step A for forming the dihydroindole C-ring of the CC-1065 / duocarmycin analog.